DELAWARE HOSPITAL NUMBER

DELAWARE STATE MEDICAL JOURNAL

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FEB 13 1948
NEWARK, DELAWARE

Official Organ of the Medical Society of Delaware

INCORPORATED 1789

VOLUME 20
NUMBER 1

JANUARY, 1948

Per Copy, 50c
Per Year, $4.00

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Entered as second-class matter June 28, 1929, at the Post Office at Wilmington, Delaware, under the Act of March 3, 1879. Editorial Office, 822 North American Building, Wilmington, 7, Delaware. Business Office, Farnhurst, Delaware. Issued monthly. Copyright, 1948, by the Medical Society of Delaware.

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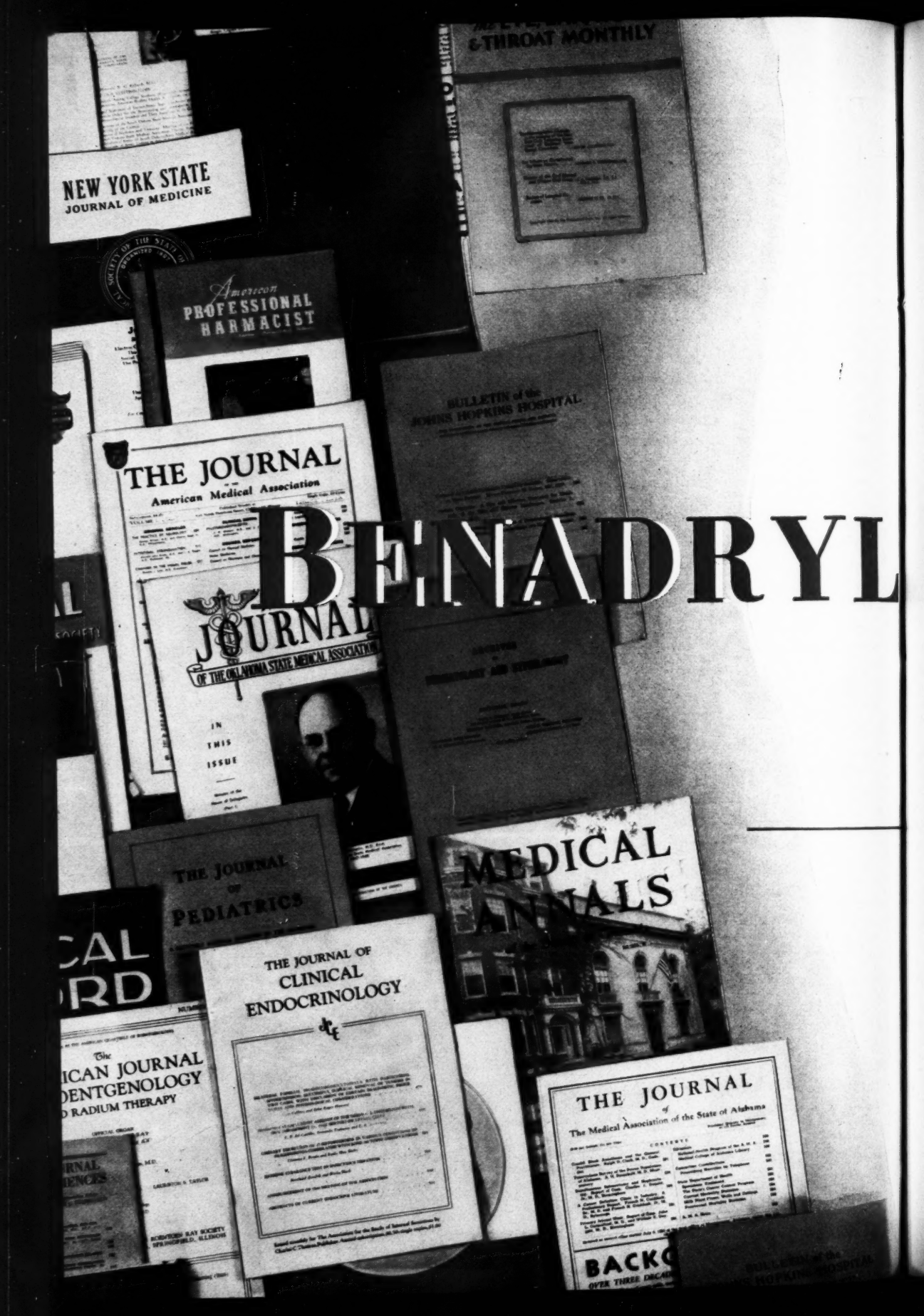
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BENADRYL
JOURNAL
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ISSUE
THE JOURNAL
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Issued Monthly Under the Supervision of the Publication Committee
Owned and Published by the Medical Society of Delaware

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GASTRIC NEURILEMOMA
Report of Four Cases

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John W. Howard, M.D.
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Neurilemomas of the stomach and of the retroperitoneal space behind the stomach are uncommon in the literature. Previously these tumors have been reported as neurinomas, perineural fibroblastoma, and sarcomas. Foot[1] presents a resume of the modern concepts of these tumors. Two views regarding histogenesis still exists. One group favors ectodermal neurogenic origin from the cells of the sheath of Schwann, and the other mesodermal fibroblastic etiology. These tumors have been more commonly reported in the region of the central nervous system and the peripheral nerves. It may be assumed properly that in the stomach these tumors might have origin in the submucous plexus of Meissner or the myenteric plexus of Auerbach. Masson[2] called the tumor a "Schwannoma," Stout[7] more properly identified this variety of peripheral gliomas as a neurilemoma. In the English literature the term perineural fibroblastoma still predominates.

Pathology and Incidence. Benign stomach tumors have been roughly estimated to make up about 5% of all gastric tumors[3]. In a series of benign gastric tumors collected from the literature, Minnes and Geschicter[3] in 1936 reported that neurofibromata constituted 10.9% of 931 benign gastric tumors. The term neurilemoma does not specifically appear, and may represent all or a portion of the tumors listed in this manner. There are two histologic types of this tumor. The Verocay type is the more characteristic because of the arrangement of the fibers with their nuclei in parallel and opposing palisades in the more typical forms (Verocay bodies), and the Antoni type which is much less orderly and more like a myxoma or a sarcoma. It is this type that rarely provides the malignant form of neurilemoma. Grossly these tumors frequently appear encapsulated and are often yellow orange or gray yellow in color. They are rubbery and firm and while they usually measure around 3 cm. in diameter, some may grow much larger.

Diagnosis Neurilemomas, in our experience, are seen more frequently in the stomach than in any other part of the gastro-intestinal tract. They occur more commonly in men, related possibly to the low incidence of stomach neoplasms in women. Patients with this type of tumor may be sympton free for years. The clinical signs are not characteristic. Hemorrhage due to ulceration occurs in about 50% of the cases[4] and is manifested by hematemesis or melena which is often the primary symptom. One reported case had[5] had melena five times in five years as the only complaint. Rarely there is a palpable gastric mass. Occult blood in the stool is common and there may be a secondary anemia.

The diagnosis of neurilemoma depends upon the roentgen rather than the clinical findings[6]. After a barium meal a neoplasm can usually be seen. Pressure signs will be noted, especially if the tumor is exogastric and is in the close proximity with other organs. If the tumor is intra-mural, a smooth filling defect will be seen. The essential diagnostic features are the smooth outlines of both curvatures of the stomach and the persistence of contractions and mucosal folds. Rarely are the curvatures involved. After a gastric meal the smooth filling defect can be seen, usually occurring on the surface near the lesser curvature, a region rich in nerve fibers. If ulceration of the lesion has occurred a large deep niche can be seen penetrating into the tumor. With the above findings, in the absence of gastric retention, neurilemoma may be suspected. However, if the tumor is in the pylorus or prolapses into

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**Resident in Radiology and Pathologist, respectively, Delaware Hospital.

the pylorus the emptying time of the stomach may be increased.

CASE 1*

J. K. Case #146676, a 56 yr. old white male was admitted to the Delaware Hospital on June 4, 1947 with the chief complaint of "tarry stools" of one month's duration, and of abdominal distress and a feeling of pressure in the upper abdomen. He gave a history of a coronary attack in 1940 which had resulted in weakness and shortness of breath after slight exertion. On examination he appeared well developed and nourished and not acutely ill. The heart was slightly enlarged. There

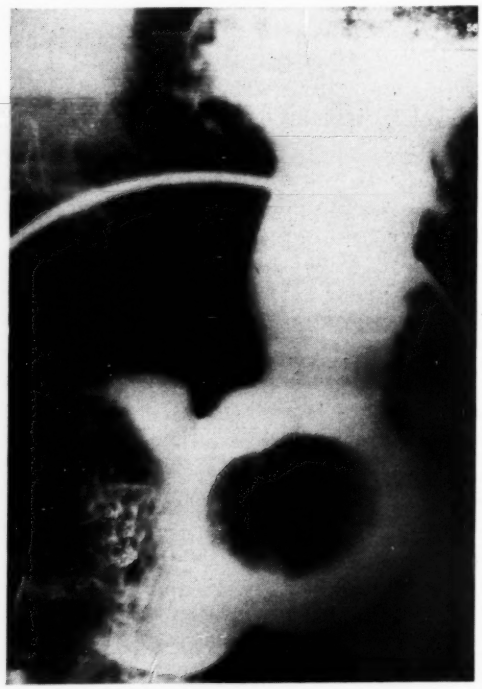

Fig. 1 — Case 1.

Radiograph demonstrating a large, spherical filling defect opposite the incisura angularis of the stomach, and lying midway between the two curvatures. No evidence of ulceration can be seen.

were no palpable abdominal masses. Laboratory studies appeared normal except for a WBC of 3500 with a normal differential. Stools were negative for occult blood.

Roentgenological examination on admission reported a normal esophagus and the stomach in the normal position. Fluroscopically a large spherical defect was seen opposite the incisuria angularis of the stomach, lying approximately mid-way between the two curvatures of the stomach. This lesion could not be brought into profile in any position, and it could not be determined whether it was on the anterior or posterior wall. Peristalic waves passed thru both curvatures around the lesion. Compression films showed no evidence of ulceration. The pre-pyloric region and the duodenal cap both appeared to be normal. Radiographs showed a five centimeter defect in the same area reported. (Fig. 1). At five hours the stomach was empty and the meal had reached

Fig. 2 — Case 1.

the transverse colon. The lesion appeared benign, but in the presence of melena was considered malignant until proven otherwise.

On June 16, 1947 at operation, the anterior gastric wall was found distorted by a bilobate type of tumor which was growing from the anterior wall of the stomach, and was invading the lumen but not the anterior wall. A subtotal gastrectomy and a Polya-Hoffmeister

*From the service of Dr. J. C. Pierson.

anastamosis were performed. Pathological report #47-9331 grossly reported a round raised tumor mass measuring 4 x 3 x 2 cm. in the mid-portion of the lesser curvature which was covered by smoothed out mucosa with a 3 mm. ulcer at the apex (Fig. 2). Section revealed a homogeneous grey red moderately firm tissue with areas of hemorrhage. Microscopic section (Fig. 3) revealed whorls and interlacing bands of spindle shaped cells with elongated nuclei. In areas the cells were quite dense, while in other areas the structure was quite loose. In the latter the cells were large with a clear cytoplasm and small hyperchromatic nuclei suggesting mucoid tissue. In some of the more solid areas there were suggestions of "Verocay bodies."

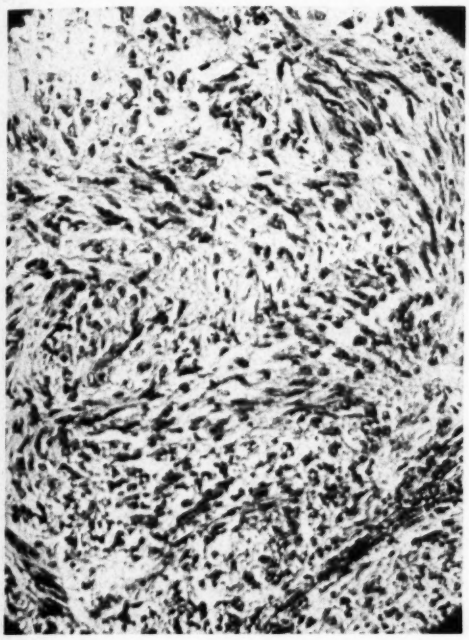

Fig. 3 — Case 1.

The post-operative course was uneventful and the patient was discharged free from symptoms on July 2, 1947. Except for a mild attack of hepatitis in November 1947, the patient has been well and free of symptoms as of January 1948.

CASE 2*

A. G. W. Case #144985, a 51 year old colored male was admitted to the Delaware Hospital on March 21, 1947 with the complaints of fever, chills, and left chest pain since morning. During the preceding year he reported that he had been eating less because his abdomen was enlarging and he thought he was getting fat. He also had noticed small lumps on his abdomen during the year. There had been no abdominal pain, indigestion or change of bowel habit. Examination revealed a well developed and well nourished colored male in no apparent distress. There was an area of pneumonia in the left chest. The superficial abdominal veins were dilated. On inspection a smooth appearing mass could be seen filling the entire left upper quadrant and on palpation was nodular, non-movable, non-tender, and about the size of a cantaloupe. The mass moved downward somewhat on deep inspiration and extended over the mid-line. Percussion over this area was dull, gastric tympany was absent, and peristalsis was normal. Laboratory examinations revealed a slight anemia and an icterus index of 8.

Roentgenological examination verified the pneumonia and showed an elevation of the left diaphragm by an abdominal mass. A flat plate of the abdomen showed obliteration of the upper two-thirds of the left psoas muscle shadow by a large opacity which also depressed the gas in the left half of the transverse colon. A retrograde pyelogram showed the left kidney pushed downward to the level of the 5th lumbar vertebrae with obliteration of the upper calices.

A gastro intestinal study reported the esophagus somewhat dilated. With the patient in the upright position the barium passed rapidly to the middle third of the stomach which was narrowed and showed a constant deformity along its greater curvature. (Fig. 4). The pyloric end of the stomach filled normally. Peristalsis began promptly and progressed normally thru the lower end. Serial films showed the same defect and narrowing in the upper half of the body of the stomach. Five hour films showed the head of the meal in a very low transverse colon. By means of a barium enema most of the loops of the colon were demonstrated to be below the iliac crest.

Following adequate response of the pneumonia to therapy, an operation was performed on 4/4/47. A massive nodular tumor was

*From the service of Dr. E. G. Laird.

Fig. 4 — Case 2.

Radiograph taken with the patient in the upright position showing a filling defect and deformity along the greater curvature of the stomach. The upper third of the stomach is narrowed and the lower esophagus is dilated.

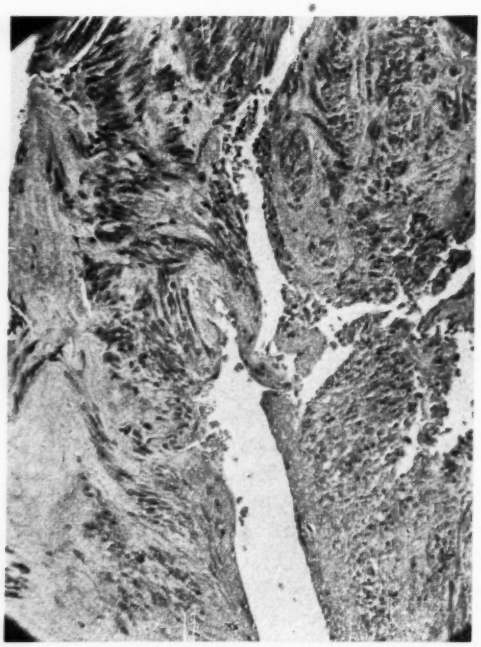

Fig. 5 — Case 2.

found predominately situated in the retroperitoneal space between the region of the stomach and the transverse colon. It surrounded the portal vein and left kidney and the stomach. As obstruction was not present a biopsy was taken from the gastro-colic omental area and the abdomen was closed without further surgery. Pathological report #47-8873 (Fig. 5) microscopically showed a tumor consisting of interlacing strands of wavy cells producing an abundant intercellular stroma. Many elongated nuclei were arranged in parallel and opposing palisades with dense masses of fibrils between the rows of nuclei.

The post-operative course was uneventful and the patient was discharged April 19, 1947. The patient has not returned to Clinic but is reported working and well in January 1948.

CASE 3*

L. O. Case #139678, a 54 year old white male who had been a mute for four years supposedly following a blow to the left side of his head several years before. Within a period of two years before admission to the Delaware Hospital on July 15, 1946 he had developed a right hemiplegia and almost total loss of hearing. Marked urinary infection followed incontinence and cystic calculi. Hospitalization was provided for terminal care. Autopsy 46-143 on September 29, 1946 showed, in addition to the marked emaciation and debility associated with a prolonged septic course, an 8 cm. meningioma located in the right temporoparietal region and a 4 cm. left acoustic neurofibroma. On examination of the stomach a stony hard papillary white mass which narrowed the pylorus was found and which extended thru the wall to present on the outer surface in the form of numerous pedunculated firm tumor masses measuring up to 1.5 cm. in diameter. Microscopic examination of the gastric tumor revealed numerous

*From the service of Dr. B. S. Vallett.

well defined Verocay bodies making up the bulk of the tumor. (Fig. 6).

Fig. 6 — Case 3.

CASE 4*

B. J. Case #145981, a 50 year old white woman admitted to Delaware Hospital May 5, 1947 complaining of dyspnea and curious crippling cramps over the left arm, left chest and left abdomen. These symptoms had begun eight months previously and were precipitated by the slightest exertion. There had been 30 lbs. weight loss in the past six months and slight jaundice for one week. Examination revealed a chronically ill appearing patient, slightly icteric with a mass in the mid-epigastrium. Laboratory studies revealed a marked anemia.

Roentgenographic findings reported a gross filling defect and irregularity of the cardiac end of the stomach extending downward along the upper third of the lesser curvature of the stomach. (Fig. 7). There was no gastric retention. A chest film revealed elevation of the left diaphragm. Vertebrae and left shoulder showed no evidence of tumor.

An exploratory operation was performed on May 22, 1947 and the upper portion of the stomach was reported rubbery, firm and carcinomatous with spread into the peritoneum, over the spleen, and under the surfaces of the

Fig. 7 — Case 4.

Radiograph showing a gross filling defect and irregularity of the cardiac end of the stomach.

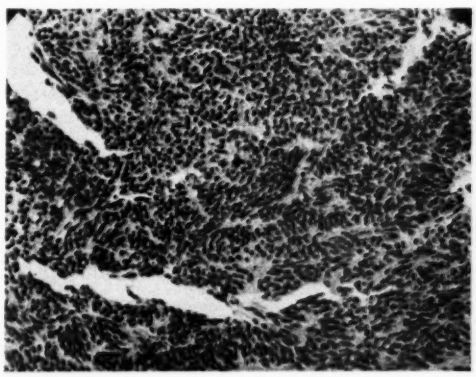

Fig. 8 — Case 4.

left diaphragm where large amounts of friable tumor tissue were scooped up and sent for histological study. Tumor nodules were also palpated in the omentum and liver. The condition was considered inoperable and the abdo-

*From the service of Dr. D. J. Preston.

men was closed. Pathological report #47-9188 revealed whorls of interlacing spindle shaped cells forming Verocay bodies and suggestive rosettes. (Fig. 8). Patient subsequently died at home in July 1947.

SUMMARY

The incidence and the etiology of neurilemomas are reviewed.

Roentgenological findings associated with gastric neurilemomas are presented.

Four cases of neurilemomas, probably of gastric origin are presented with roentgenological findings demonstrating gastric lesions.

Microscopic pathology appeared typical in all four cases.

Characteristic roentgenological findings should suggest the diagnosis of gastric neurilemomas.

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PERINEAL AND VAGINAL TOTAL CYSTECTOMY

BRICE S. VALLETT, M. D.*
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In a consideration of the operation proposed by the title of this report the indications should first of all be set forth. Preliminary transplantation of the ureters simplifies total cystectomy. In the male one important indication is to remove an adequate amount of urethra, as there has been recurrence in the urethra following suprapubic total cystectomy. In perineal total cystectomy there is a lesser degree of shock, and drainage is more dependent. There is also less likelihood of injuring the rectum, and the arteries to the seminal vesicles can be more easily controlled. Previous abdominal operations with or without complications may lead one to select the perineal route as in the case previously reported.[1]

In the female, when the urethra and vagina, are invaded by vesical cancer, the vaginal approach is then better and easier. Uterine involvement may demand vaginal hysterectomy at the same time. The same indications apply here as in the male.

A recent case, B. R., #147190, will exemplify some of these points. A female, aged 58 and the mother of five children, had had dysuria for more than one year and prior to admission to the hospital on June 17, 1947 had exhibited gross blood in the urine. Cystoscopy revealed a tumor of the bladder involving the vesical neck, the right lateral wall, and the urethra. Bimanual examination under spinal anesthesia was done at the same time and definite fixation of the growth to perivesical structures was not found. This maneuver is one advocated by H. J. Jewett[2] of Baltimore to determine operability. An excretory urographic study showed good bilateral renal function despite back pressure from the tumor. The cystogram showed a gross filling defect corresponding to the same area where tumor was visualized at cystoscopy.

This composite picture indicated total cystectomy and on July 8, 1947 through a low left paramedian abdominal incision the ureters were transplanted into the sigmoid by the Coffey #1 technique. An enlarged retroperitoneal lymph node adjacent to the left common iliac vessels was removed for biopsy, but revealed no metastasis on microscopic section. Preoperative ex-rays of the chest and abdomen revealed no evidence of metastases. The postoperative course was uneventful, aside from a mild degree of abdominal distension, and urine drained satisfactorily from the rectal tube.

Twenty days later (July 28, 1947) the cancer-bearing organ was removed through an anterior vertical vaginal incision which ran from just in front of the cervix up to and encircled the urethra. A perineal catheter drain with large inflatable bag was introduced through the urethra into the bladder to act as a tractor. Grant of Louisville has described the use of such a bag in doing perineal prostatectomy as it is less traumatizing than the metal prostatic tractor. Beginning at the urethra and working backward, all the while adhering closely to the bladder wall, the dissection is surprisingly simple. In this case there was thickening of the right inferolateral ligament and a biopsy was taken from this site, microscopic section revealing no malignancy.

*Urologist, Delaware Hospital.

After removal of the bladder two Penrose drains were placed in the dead space and the anterior vaginal wall closed around them using interrupted sutures of medium heavy black silk. The operation consumed one hour and the patient was returned to her bed in good condition.

Pathological Report S-47-9583 grossly described the removed bladder as containing a 5 x 6 cm. reddish grey fungating mass surrounding the mucosal neck of the bladder and extending into the urethra and infiltrating the bladder wall. Microscopic examination revealed papillary filaments of pleomorphic transitional epithelial cells and nests of poorly differentiated epithelial cells which have invaded deep into the stroma. The nuclei of these tumor cells are hyperchromatic and exhibit numerous mitotic figures. Necrotic areas are present in the mucosa and stroma. The blood vessels are congested and focal inflammatory changes are in evidence. Diagnosis: epidermoid carcinoma of the bladder.

The patient improved gradually following this second operation and in four days was back on a full diet. Just before discharge from the hospital (three weeks after operation) another excretory study was made. Dye appeared in both renal pelves in the 5 minute films, while the 20 minute films showed good concentration on both sides. Both renal pelves showed a moderate degree of hydronephrosis. At the time of discharge (August 22, 1947) patient had good urinary control and was able to retain the urine for three and four hours at a time.

Marshall and Schnittman[3] recently reported five cases of vaginal total cystectomy and also describe their operative technique. They state "this operation removes a block of tissue composing all of the bladder and urethra plus the vestibule, the upper wall of the vagina, all the subvesical tissues, and most of the perivesical fat. The richly lymphatic tissue between the trigone, the vagina, the cervix, and the lower ends of the ureters is removed with the specimen. Particularly notable has been the patient's ability to withstand the procedure easily and their post-operative comfort has been most impressive." Unless there is gross evidence of tumor infiltration into the anterior vaginal wall or periurethral tissues a less extensive incision than the one employed by the authors mentioned above will serve the same purpose. Jewett feels that it is impossible to remove the necessary amount of perivesical fascia by the perineal and vaginal routes. While this statement is theoretically noncontroversial, in practice selected cases may do better by these routes.

Finally, only by judicious use of blood transfusion, penicillin, streptomycin, and the sulfonamides can one hope to achieve success in these cases.

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KERNICTERUS:
A Review of the Literature, with Report of Two Cases*

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Wilmington, Del.

Recent advances in hematology, initiated by Levine in 1941,[1] after discovery of Rh by Landsteiner and Weiner in 1940,[2] have enabled clinicians to recognize the entity of erythroblastosis and its importance in obstetrics. Many are now familiar with the infant suffering the crisis of erythroblastosis, the eminence of their demise, and often needed exsanguination or supplementary transfusions.

Because there undoubtedly will be more survivors of erythroblastosis in the next decade, the clinician and especially the pediatrician will be confronted by survivors of therapy. The incidence of kernicterus in survivors of erythroblastosis varies in the literature. (Table I).

Kernicterus, originally called nuclear jaundice by Orth[3] in 1875, was established as a clinical entity in 1933 by Zimmerman and Yannet,[4] who associated erythroblastosis and neonatal jaundice with signs of central nervous system involvement. Survivors showed symptoms of mental retardation and basal cell ganglion injury. Nuclear jaundice was demonstrated at necropsy of these cases. Yannet[5] has shown that the incidence of mother-child Rh blood type incompatibilities were significantly higher in a group of undifferentiated

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**Resident in Pediatrics, Delaware Hospital.

mental defectives than in a control group of mongols, infantile spastic diplegias, etc.

Docter[6] describes kernicterus as: "pigmentation and degeneration of nerve cells of the brain, particularly the basal ganglion." Clinically, manifestations of this entity are: extrapyramidal spasticity, convulsions, delayed motor functions, incoordination, athetosis, chorea, lethargy, moderate opisthotonos and mental retardation with history of severe neonatal jaundice and anemia, associated with incompatibilities of Rh factor between mother and infant. Bluish green discoloration of deciduous incisors is common. Lethargy tends to subside with recession of jaundice.

Pathological changes are not usually demonstrable in stillborns,[7] but only those surviving several days or more. Grossly, pale yellow to deep orange discolorations of localized areas are found in varied areas of the brain. This is conceded by most authorities to be bilirubin. Histologic preparations are difficult, but generally show absence of Nissl substance, or groups of swollen cells.

Theories of pathogenesis of kernicterus are variable. No cases are known to have occurred following obstructive jaundice.[5] Attempts to reproduce kernicterus in animals by injection of bilirubin are unsuccessful, unless accomplished in conjunction with brain injury or exposure to x-ray.[7] Leonard[8] and Stiller[9] feel there is no ratio between extent of nuclear jaundice and clinical manifestations. Weiner[10] suggests agglutinated erythrocytes plug brain capillaries causing anoxemia with death of ganglion cells and straining by bile pigments in the circulation. Vaughn[11] feels there is sufficient evidence that blood destruction is not the primary determinant of nuclear damage but immaturity, vascular injury, altered antigen antibody reactivity, and intrapartum transfer of antibody may play possible roles. Darrow and Chapin[12] propose kernicterus is due to anoxia, to intoxication, or to direct sensitization of nuclear neurons, the effected cells showing greater avidity for circulating pigment than surrounding brain tissue. They state the theory of bilirubinemia producing selective injury to the brain after erythrocyte destruction is open to question.

TABLE I GROUP CASES OF KERNICTERUS IN ERYTHROBLASTOSIS

Group	No. Cases	Deaths	Survivors	Kernicterus Died	Kernicterus Alive
Stiller (9)	35	6	29	2	4
Vaughn (11)	72	25	47	16	4
Docter (6)	20	7	13	6	5
Leonard (8)	55	19	36	5	1

CASE #1

A. S. #148054 white male infant, aged 8 months, was admitted to Delaware Hospital August 5, 1947 with chief complaint of fever of one week's duration. It had received sulfadiazine and penicillin in beeswax and oil without response. Anorexia was marked. P. M. H.: Second sibling born spontaneously at full term in October 1946. Birth weight, 6 lbs. 6 oz. (4636 grams). Severe jaundice was present at 3 days and a poor prognosis was given. The child would never nurse from a bottle. It was fed liquids by a spoon. Upper incisors erupted at 6 months. The head could not be held erect nor could he sit at 8 months. The diet included pureed foods, whole milk and adequate supplementary vitamins. Family History: Father and older brother living and well. Mother living and well. She had no previous transfusions or abortions.

Physical Examination Dehydrated, slightly dyspneac, white infant, weight 12 lbs. 8 oz. (9090 grams) Temperature 102°F. rectally. Skin: irregularly distributed macular rash on back; blemishes of pin point size on right arm, resembled petechiae. Anterior fontanelle was soft, not bulging. Alternating lateral strabismus was noted. Sight was questioned. Pupils were round, equal, and reacted slowly to light. Four upper incisors and two lower incisors erupted, blue green in color. Nasopharynx was reddened. Chest was dull over right base with bronchial breath sounds and diffuse coarse rales. Heart was normal.

Neurological Examination Bilateral choreo-athetotic movements present in both upper extremities. Mild nuchal rigidity was present. Tendon reflexes were hypotonic bilaterally in biceps, triceps, patella and Achilles tendon, and abdomen. Koernig, Gordon signs were positive.

Laboratory Hemoglobin 9.5 grams, (60%); leukocytes 11,800; polymorphonuclear 42% with 7 band cells, lymphocytes 35% and monocytes 3% with moderate hypochromia. Serum calcium was 11.6 mgm% and phosphorus 3.4 mgm%. Because the fever was prolonged and was present with evidence

of pneumonia and neurological signs, meningitis was considered as a possibility. Lumbar puncture revealed: clear, colorless fluid with 175 mm. H_2O pressure. There were less than 1 cell/cu mm. and slight trace of globulin with Pandy reagent. Spinal fluid sugar was 84 mgm% and chlorides 680 mgm%. It was sterile after 74 hours culture.

Normal temperature was obtained in 36 hours by administration of 50,000 units of penicillin every 3 hrs. and intravenous glucose (5% in physiologic saline solution). Neurological signs remained as described. Feeding was extremely tedious. Further examination on August 11, 1947, ten months after delivery, revealed the child was Rh positive and its mother was Rh negative with early antibodies present with Rh_1 cells in dilution of 1:64 and with Rh_2 cells in dilution of 1:512. Blocking substance was present in dilution of 1:256 with Rh_1 cells and 1:512 with Rh_2 cells. The child was discharged August 13, 1947 with final diagnosis of broncho-pneumonia and kernicterus.

CASE 2

G. S. #144389. The patient was born February 16, 1947 at 38 weeks gestation by breech delivery and weighed six pounds and six ounces (4.6 Kg.). No physical abnormalities were noted. He was the second living sibling. No previous abortions or transfusions were known. Jaundice became prominent on the fourth neonatal day. Splenomegaly was absent.

On February 23, 1947, the infant was admitted to the Delaware Hospital with the diagnosis of erythroblastosis. The infant was lethargic and dehydrated; skin and sclera were icteric. Weight on admission was five pounds, eleven ounces. (4.1 Kg.) Posterior fontanelle was closed. Anterior fontanelle was soft, not bulging, and normal size. Pupils were round, equal and reacted to light. No spasticity or paralysis was noted. Splenomegaly was absent. Hemoglobin was 17.6 gms. with 5 million erythrocytes/cu.mm. No nucleated erythrocytes were noted in any smears. The baby was Rh positive. The mother was Rh negative, and on March 3, 1947, seventeen days postpartum, early antibodies were demonstrated with Rh_1 cells in dilution 1:2 and with Rh_2 cells in dilution 1:1. Blocking substance was present with Rh_1 cells in dilution 1/256 and with Rh_2 cells in dilution 1:512.

Nursing from a bottle was difficult. A high pitched cry was prominent. Dehydration was treated with intravenous administration of glucose (5% in physiological saline). No blood was given. On February 25, marked retraction of the head toward opisthotonos, and clonic movements of the extremities with moderate spasticity was noted. These, and jaundice decreased spontaneously by March 13, 1947. Feeding was easier and the infant was discharged March 19, 1947, weighing six pounds, ten ounces. Erythrocyte count was 4.8 million with 15.3 gms.% hemoglobin.

On April 21, 1947, clonic movements returned in the left arm and gradually involved the whole left side. Convulsions occurred periodically and resembled march seizures of the left side. Opisthotonos, irritability and almost continuous crying were also present. The patient was readmitted to the Delaware Hospital on April 24, 1947 for study and treatment of its feeding problem. There were: bilateral clonic movements, more marked on the left side and moderate spasticity of extremeties opisthotonos, but no nuchal rigidity. Clonic movements resembled epileptiform seizures without incontinence. These could be relieved momentarily by forced movement. Phenobarbital gave temporary relief. Weight on this admission was nine pounds, nine ounces. Blood count was within normal limits for his age. The infant was discharged unimproved on May 9, 1947 with the final diagnosis of kernicterus.

At the age of five months, the infant was readmitted to Delaware Hospital because of difficulties at home. It weighed eleven pounds, fifteen ounces (5.3 Kg) Vision was questioned, but corneal reflexes were normal. Clonic movements with spasticity were still present. He could not hold his head erect or raise the head from prone position. Erythrocytes were 4.8 million/ cu.mm. with 12.9 gms.% hemoglobin.

Intermittent febrile attacks occurred between July and October, at intervals of about fourteen days and lasted two to ten days with temperature between 102° and 107°F. At these times, convulsions were worse and more

frequent, and did not respond to phenobarbital. The only notable finding in all instances was erythema of nasopharynx and coarse inspiratory rales over upper hemithoraces. Lumbar puncture during one such febrile attack revealed clear colorless fluid with 3 wbc/cu. mm., normal globulin, and no growth on culture after 72 hours. Urinalysis and urine cultures were sterile during these attacks. Convulsions and spasticity were often absent for several days following these attacks.

At eight months a neurological and psychological examination was done to institute proceedings for admission to the Delaware Colony for the Feebleminded. The results were as follows:***

TABLE II

Test	Chronological age	Mental age	Quotient	Normal
Vineland Social Maturity	0-8 mos.	0-2.1	26	80-120
Cattell Infant Scale		0-2.6	32	80-120
Gesell Schedules		0-2.2	27	80-120

Patient remains in unvarying bodily position during the examination. Range of movement is distinctly limited. He has defective control of most muscles and is therefore unable to use them for adaptive responses. His hands are predominately clenched. Grasp of objects placed into his hands is delayed and accompanied by twitching of the small muscles of the hands. He extends and flexes his fingers from time to time, but makes no attempt to move his arms or to play with them.

While stimulated tactually, visually, and auditorily he stops sucking on the bottle, indicating that there is passive response to simple and intense stimulation. His eyes follow the pencil in a horizontal plane. They also follow moving people and stare at shiny and bulky objects in the distance. There is an abortive response to bell sounds. Affective responses are elicited by active bodily manipulation. As far as can be determined, there is complete absence of emotional expression to social approach or to anticipated feedings. He is fretful and uncomfortable when held up or carried by the nurse. The head is limp and droops as soon as external support is removed.

The general mental development at this time is seriously retarded. His motor functions are among the most backward. His adaptive responses are somewhat higher than are motor activities, but no ability is better than an imbecile and he is classified as feebleminded.

***Courtesy of Dr. M. A. Tarumianz, Director, Mental Hygiene Clinic, Delaware State Hospital, Farnhurst.

Neurological Examination. This 8 months old infant rests almost inertly in bed, unable to move himself or even turn his head. The pupils are paradoxical, varying from very small to medium-large, responding to light and immediately expanding. Tendon reflexes are enfeebled and all extremeties are moderately spastic.

Impression. Marked mental deficiency due to organic cause.

The patient's condition is approximately the same at ten months. He is awaiting admission to the Delaware Colony for the Feebleminded. He weighs twelve pounds (5.4 Kg.) is able to eat solid food and makes some attempts at movement.

SUMMARY AND CONCLUSIONS

1. Kernicterus will undoubtedly be seen more frequently in practices of pediatricians and other clinicians due to greater number of survivors of erythroblastosis fetalis.

2. Pathogenesis of kernicterus is arbitary, but is a definite sequella of erythroblastosis, deposition of bilirubin in the brain, and ganglion cell destruction.

3. Survivors show various neurological findings, particularly extra-pyramidal tract disorders and mental retardation. Those autopsied show patchy areas of nuclear pigmentation which, however, is thought to have no ratio to the extent of neurological disturbance.

4. Two cases of kernicterus are reported.

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RAT-BITE FEVER DUE TO STREPTOBACILLUS MONILIFORMIS*

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Rat-bite fever, after a 1 to 10 day incubation period is characterized by a sudden onset, beginning with fever, chills, and severe headache. A maculopapular rash on the hands, arms and feet follows in several days along with a recurrent or relapsing type of fever, and arthritis. There is generally an absence of ulceration at the site of the rat-bite.

Sufficient evidence has accumulated to indicate that the important etiological agent is an extremely pleomorphic micro-organism, *Streptobacillus moniliformis*, first adequately described by Schottmuller in 1914. Much confusion has occurred in its nomenclature, at least three different names having been assigned to similar, if not identical, micro-organisms since its original description. The streptobacillus (the name indicating chains of bacilli interpersed with beaded swellings) is apparently a normal inhabitant of both wild and laboratory rats, and can be isolated with some degree of consistency from the blood and joint fluid of an infected human. In broth cultures of such blood the organism grows in small colonies, described as "cotton" or "fluff balls," resting upon the surface of the sedimented red blood cells. Smears of these colonies, as well as of those growing in a solid infusion agar containing 20 to 30 per cent serum or ascitic fluid, show gram-negative rods and filaments containing globules or swellings and granulations. After several days incubation of the agar plate, dense areas, appear under the colonies, which are visible only by low power (70-90x) magnification. By washing off the earlier growth of streptobacilli, these dense areas, called L_1 forms pass through ordinary bacterial filters, and resemble in this respect similar forms of the pleuropneumonia group. Brown and Nunemaker,[1] in an excellent summary of the bacteriology of *S. moniliformis*, are of the opinion that the L_1 components and the streptobacilli are both stages in the life cycle of the same organism, the L_1 component being a survivor of moderately adverse growth conditions.

There have been approximately 40 bacteriologically proved cases of rat-bite fever due to *S. moniliformis* reported in the American literature since 1916, occurring in 16 states and the District of Columbia. It is believed that this is the first case to be reported from Delaware.

CASE REPORT

The patient, W. F., #143863, a 31 year old white male, who was employed as an animal house keeper in a nearby research laboratory, was admitted to the Delaware Hospital on July 11, 1947, complaining of a severe occipital headache, chills, fever, and anorexia. These headaches had been of 2 months duration, and several days before admission the patient had a "cold." He had lost 5 to 6 pounds of weight during the previous week. A past history of arthritis and possible peptic ulcer was elicited. On the day of admission the patient reported a non-itchy rash on the feet, hands and fingers and stated that he had recently been bitten by ticks.

Physical Examination: On physical examination slight nuchal rigidity was noted along the hyperactive knee reflexes. Eyes, ears, heart, and lungs were not remarkable, and the liver and spleen were not felt. There were numerous maculopapular eruptions on the ankles, dorsa and soles of the feet, as well as some petechiae, none of which faded on pressure. The temperature was 100.6 F., the pulse 82, respirations 22, and blood pressure 96/36. The clinical impression was Rocky Mountain spotted fever, lymphocytic choriomeningitis, central nervous system lues, or purulent meningitis.

Laboratory Studies: Laboratory studies showed a hemoglobin of 13 grams, 83 per cent, white blood cells 7,600 with 78 per cent polymorphonuclears and a slight shift to the left. The admission urinalysis was normal, blood serology negative, and no agglutinins could be demonstrated against Proteus OX19 antigen. A spinal tap resulted in a clear fluid under no increased pressure, with normal chemical findings and cytology. A 24 hour sputum specimen showed no tubercle bacilli on concentra-

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tion, and rectal and urine cultures proved non-contributory. The findings of an admission blood culture will be discussed later.

Hospital Courses: Sodium para-amino benzoic acid, 2 grams every 2 hours by mouth, was started on admission. A para-amino benzoic acid blood level the following morning showed a concentration of 8.7 mg.%. Since previous work at this hospital[2] indicated the optimum PABA blood concentration to be

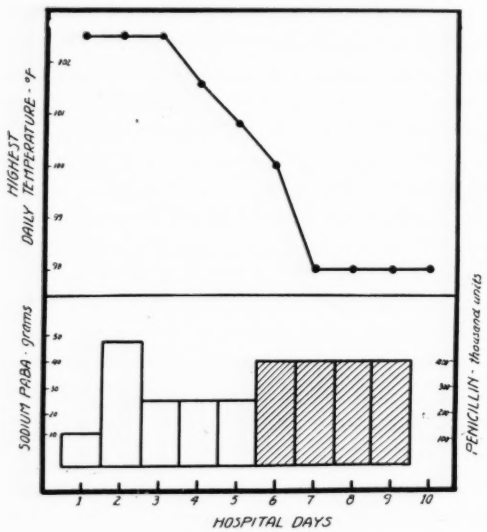

Fig. 1 — Course of Illness.

between 30 to 60 mg.%, the drug was increased to 4 grams every 2 hours. After a 24 hour period at this higher dosage, a blood concentration of 40.2 mg.% was attained. The dosage was thereafter dropped to the original amount and continued for 4 days until July 16th, and, as the chart will indicate, without apparent effect on the temperature course. A total of 132 grams of Na PABA had been administered to date, more than enough to demonstrate some clinical response. This therapeutic failure encouraged some doubt as to the accuracy of the original diagnosis.

A repeat Proteus OX19 antigen agglutination performed 6 days after the first test, again gave negative results. The rash had become apparent on the abdomen, and the macules appeared fewer in number. The headache had diminished somewhat in intensity, nuchal rigidity and still present, and the patient showed little symptomatic improvement.

On July 16th the laboratory reported that an organism had been isolated from a blood culture taken on admission, which had been tentatively identified as *S. moniliformis.* Growth occurred only in BBL thioglycollate broth which had been inoculated with 2 c.c. of citrated blood, and was apparent microscopically (after 5 days incubation) as typical "cotton balls" resting upon and enmeshed in the sedimented red blood cells.

Fig. 2

Culture of blood in thioglycollate medium showing "cotton balls" of Streptobacillus moniliformis in sedimented red blood cells.

Smears of these "fluff balls" revealed the presence of extremely pleomorphic gram-negative organisms, with globules and swellings at

various points along the chains. Segmented forms were observed, which appeared to consist of dense material (swellings) interspersed between a clear continuous membrane. Numerous unsuccessful attempts were made to grow out the L_1 components on 20% serum agar and ascitic fluid agar plates incubated aerobically, in 10% CO_2 and anaerobically. Cultures of doubtful viability were finally sent to Dr. Ruth H. Wichelhausen, bacteriologist at Veterans Administration Hospital, Washington, D. C., along with several blood samples taken at various days of the disease for agglutination reactions with *S. moniliformis* antigen. Dr. Wichelhausen replied that "in spite of many attempts we were not able to revive your cultures"*, and that any information gained from agglutination reactions would be reported later. Despite this reply, and the inability to grow out the L_1 forms, it was felt that from morphology and growth requirements alone, a positive indictification of *S. moniliformis* could be made.

The penicillin was administered for 4 days (total dosage 1.6 million units). By the 2nd day of this therapy the maculopapular rash had gradually disappeared. The patient was discharged improved on July 22, 1947. The petetchiae, however, persisted for 10 days af discharge. Recovery was otherwise uneventful.

SUMMARY

1. A case of rat-bite fever due to *Streptobacillus moniliformis* has been reported in the state of Delaware.

2. The rash of this disease was confused with the rash of Rocky Mountain spotted fever.

3. PABA administration was of no therapeutic value in this disease.

4. A prompt and satisfactory clinical response was obtained with penicillin.

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*Dr. Wichelhausen suggests a trial method of preserving such cultures: Culture in pancreatic digest broth with 20% ascitic fluid and store in deep freeze (-15°C). She had kept one culture viable for at least 1 week without transfer.

CONTRACT NO. VAm—23104

To The Administrator of Veterans Affairs:

The Medical Society of Delaware and the Veterans Administration for the purpose of establishing and maintaining a close working relationship in order to establish a well-integrated service for providing medical care and treatment for veterans of the State of Delaware, beyond those services available to the Veterans Administration in existing Veterans Administration facilities and installations, do hereby mutually agree as follows:

(1) The Medical Society of Delaware will request all of its members to participate in a State-wide program whereby physicians in private practice in the State of Delaware will render medical services (examinations, treatments and counsel) in such cases as may be specifically authorized by the Veterans Administration.

(2) The Medical Society of Delaware will submit to the Veterans Administration a list of its members who desire to provide service for eligible veterans in the home communities of such veterans. This list may be augmented from time to time as additional physicians may indicate a desire to participate in the program. The physicians so listed will be fee designated physicians of the Veterans Administration. By notice in writing a physician may at any time request that his name be removed from the list of fee designated physicians.

(3) The Medical Society of Delaware will assist the Veterans Administration in establishing, for examinations and treatment, a list of competent specialists who meet the quaiifications of specialist of the Veterans Administration.

(4) Lists of physicians submitted by the Medical Society of Delaware will be broken down by counties or districts in order that the veterans for whom services are authorized may select a physician practicing in his home community. The choice of the physician by the veteran, provided for herein, is not applicable to examinations for pension or compensation rating purposes. Such examinations may be perfórmed only by a physician specifically designated for that purpose by the Veterans Administration.

(5)A Fees for medical services in authorized cases shall be paid by the Veterans Administration to the physician rendering the service in accordance with the Fee Schedule hereto attached, which is made a part of this agreement. The Medical Society of Delaware warrants that the rates set forth herein are not in excess of the rate of fees charged other persons who are not Veterans Administration beneficiaries for the same or comparable services. It is mutually understood that

the fees stated in the Fee Schedule represent the maximum amount that may be charged, and do not represent the amount to be paid in every case. The Veterans Administration will advise each physician of this provision and will require each physician to certify in submitting his statement of account that the fees charged are not in excess of the fees charged by him for comparable service rendered non-veterans. It is understood that unusually involved cases and services not scheduled will be subject to review and recommendation by the Medical Society of Delaware to the Veterans Administration for determination of the appropriate fee.

(5)B It is further understood that services of physicians hereunder will be so utilized that fees therefor to any individual physician will not exceed $6,000.00 per annum without the prior approval of the Chief Medical Director, Veterans Administration, Washington, D. C.

(6) The Veterans Administration will handle administrative and clerical details in connection with the authorization of examinations or treatments and the maintenance of records; and will arrange for transportation of the veteran if necessary.

(7) When authorizing treatment, the Veterans Administration will furnish to the veteran, proof of such authorization and a list of fee designated physicians in the county or district in which the veteran is located, in order that he may select his own physician for the services authorized.

(8) The Veterans Administration will review reports of examinations and services to determine their adequacy. No fees will be paid by the Veterans Administration for reports which are not acceptable to the Veterans Administration or for services rendered in unauthorized cases.

(9) The Medical Society of Delaware will establish one or more boards of review composed of physicians. It shall be the duty of such board to review reports, which are deemed by the Veterans Administration to be inadequate or which do not meet the requirements of the Veterans Administration; to recommend, at its discretion, the disqualification of any physician for further work with the Veterans Administration whose work is found by the board to be incomplete or unsatisfactory; to advise and assist the Veterans Administration on other matters within the scope of this program.

(10) It is agreed that services furnished under the agreement will be performed by licensed physicians. It is further agreed that physicians rendering services hereunder will be citizens of the United States who are doctors of medicine duly licensed to practice medicine and surgery in the State of Delaware.

(11) This agreement shall be effective from 10/13/47 to 6/30/48, and may be terminated by either party by giving (30) days written notice to that effect.

(12) This agreement, if mutually satisfactory, may be renewed indefinitely for a period of one (1) year each, upon notice in writing to the Medical Society of Delaware at least sixty (60) days prior to the expiration of each period of one (1) year, and written statement from the Medical Society of Delaware within thirty (30) days after such notification agreeing to the renewal.

(13) No Member of or Delegate to Congress, or Resident Commissioner, shall be admitted to any share or part of this agreement or to any benefit that may arise therefrom unless it be made with a corporation for its general benefit.

(14) The Medical Society of Delaware agrees that in performing this agreement it will not discriminate against any employee or applicant for employment because of race, creed, color or national origin.

(15) The Medical Society of Delaware does not propose to make any charge for any service rendered to the Veterans Administration under this agreement.

Approved and Accepted

Veterans Administration

Medical Society of Delaware

A. J. Harrison

Chief, Procurement Division

By: John F. Hynes

Secretary

(Title)

(If bidder is a corporation, Form 1264 must be filled out and attached to the contract)

When a physician encounters an infant or child with a positive tuberculin test, he has six clear-cut responsibilities: he must classify or describe the lesion, judge activity, determine communicability, seek the source of infection, make recommendations for therapy based on specific objective data and, last, follow each patient carefully at frequent intervals at least until all evidences of activity have subsided or until resolution of the initial lesion is completed. R. V. Platou, Am. Rev. of Tbc., April, 1947.

+ Editorial +

DELAWARE STATE MEDICAL JOURNAL

Owned and published by the Medical Society of Delaware, a scientific society, non-profit corporation. Issued about the twentieth of each month under the supervision of the Committee on Publication.

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Footnotes and bibliographies should conform to the style of the Quarterly Cumulative Index Medicus, published by the American Medical Association, Chicago.

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Subscription price: $4.00 per annum, in advance. Single copies, 50 cents. Foreign countries: $5.00 per annum.

VOL. 20 JANUARY, 1948 NO. 1

MORE NURSES NEEDED

Our latest information is that about 42,000 more nurses are needed in this country merely to meet the existing shortage. In addition, some 60,000 will be needed to meet increasing demands. According to *Hygeia*:[1]

> A survey made by the American Hospital Association indicates that the number of nurses necessary to supply the needs of the hospitals and the people of the United States is 360,000. Over 90,000 nurses are needed for private duty nursing in which one nurse takes care of one patient. At present almost 42,000 nurses are needed to meet the shortage that prevails; probably at least 60,000 are needed promptly to meet increasing demands that will come with new hospitals and new services for nurses.
>
> Various reasons have been alleged to be responsible for the existing shortages. Before the war nurses worked in many instances a 12-hour day for six days a week. Now throughout much of the United States they work eight hours a day five days a week. This alone would mean almost twice as many nurses to meet the same needs . . .

In 1945, according to the same source, some 16 million patients entered the hospitals, as compared with 10 million in 1940. New hospital construction is under way now, and more is anticipated. Hospitalization insurance is spreading rapidly and will probably increase the demands for beds.

Under the circumstances, adequate nursing care becomes more and more a matter of concern, particularly with regard to bedside nursing. Whereas this nursing shortage is of vital interest to the medical profession, it should be of even greater concern to the public. In the final analysis, nurses must be recruited from the population in general; the medical profession cannot supply them although it can help instruct them. Why is there not a sufficient incentive for young women to study nursing?

> During 1945 a careful survey was made of medical and public opinion regarding the profession of nursing. The general belief seemed to prevail that the nursing profession is desirable but that it offers too little reward to those who practice it and too high a cost to those who need it. This is like the situation in which an irresistible force meets an immovable object. How to reconcile the two aspects of this situation is an exceedingly difficult problem.
>
> The profession of nursing today includes far more than just taking care of the sick. Nurses have positions involving administrative responsibilities. They are concerned with education. The career of a nurse is considered suitable preparation for specialized training in physical therapy, public health, and such fields as psychiatric, orthopedic, surgical, and obstetric nursing. The demand for properly qualified nurses is so great that a girl who completes her education in nursing need never be without work once she has secured a license to practice . . .

It should be conceded that in recent years many more careers in business and industry have become possible for women. Thus the field of competition has been enlarged over the time when nursing and teaching were, generally speaking, about the only careers acceptable.

> The minimum educational requirements of most schools of nursing is graduation from high school. Some nursing schools require one or more years of college work. In general students are admitted only when they have been in the upper third of the class. The preferred age is 20 to 25 years but 18 years of age is considered acceptable in a good many schools. Thirty-five is considered the upper limit. Some schools of nursing offer a combination four- or five-year program which includes a diploma for nursing and a college degree. These schools will admit high school graduates at 17 years of age.
>
> The great number of nurses who get married

1 Dec., 1947

> soon after entering the profession is an indication that this is one profession which is excellent preparation for marriage. The girl who is trained as a nurse has several advantages over girls in other occupations when it comes to contact with the susceptible male. . .

It would seem that the best approach to the problem of getting more nurses would be an intensive campaign by the nursing profession itself. Unlike the weather, about which very few do anything but talk, something can be done, but it will take hard work. First, the nurses themselves will have to "sell" nursing as a career to many more young women and their parents. To be convincing, this will mean personal contact, perhaps in the hospital, often in the home, sometimes by personal appearance at school assemblies in cooperation with local school authorities.

Nursing associations will have to initiate campaigns of public education, in women's magazines, in the press, at meetings of women's clubs.

The national and the several state medical societies can be of great assistance. Dr. Edward Bortz, president of the A.M.A., has already appointed a committee to survey the nursing problem in the United States. The state medical societies through the cooperation of their women's auxiliaries can and assuredly will assist.

Says *Hygeia* further:

> Much discussion has been going on in medical and nursing circles as to the desirability of educating more practical nurses. The excellent work the nurses' aides did during the war has emphasized this possibility. The criticism is made that professional nurses have raised their educational standards and are getting far away from bedside nursing. In Michigan the State Board of Education in cooperation with medical and nursing organizations has established six practical nurses' training centers to educate such nurses. For a number of years Detroit has had a similar project. These practical nurses are recruited from the senior students in high schools. The teachers are registered nurses on high school faculties. Practical nursing will be a part of the vocational educational system. Standards for practical nursing systems will be established. The leaders who are developing this plan assert that nurses of this type will be able to do from 80 to 90 per cent of the ordinary bedside nursing in hospitals. This may be the answer to the major portion of the problem.

While more practical nurses are certainly to be desired, the primary objective should be the stimulation of young women by all available means to consider the full training course. In our view this is primarily the obligation of the nursing profession itself with all the assistance organized medicine and its individual physicians can summon.

Editorial, *N. Y. St. J. M.*, January 15, 1948.

THE VOLUNTARY HOSPITAL

We are reprinting herewith, slightly abridged, a statement received from the president of the Board of Trustees of one of the oldest and most respected voluntary hospitals of New York City. It is of the 400-500 bed class and probably typical of the situation elsewhere in the country. Seriously, it makes our blood run cold. Is there one among us who remembers what the term "voluntary" means? "Done, acting, able to act, of one's own free will, not constrained."

In days when people had money to leave they left it first to their children, then to some charity of their own, and often a final sizable amount to a voluntary hospital. The bequest to the hospital was a genuine response to the feeling, more prevalent in those days than the "liberals" of nowadays would have us think, that money carried with it responsibility and that one of the first of those responsibilities was the decent care of the sick poor.

Now read

> The voluntary hospitals are in a very difficult position, and one which might well cause many of them to close if the conditions do not change.
>
> The hospital is efficiently run and has a fine reputation. In spite of its age and reputation it has only approximately $1,000,000 of endowment and reserve working funds of not more than $200,000.
>
> In spite of the fact that the fund-raising campaign has resulted in twice as much money being contributed this year, rising costs have used up this money faster than it could be accumulated, with the result that the meager working capital of the hospital is constantly being eaten into.
>
> There are only three or four hospitals in the city that will be able to endure such a strain for any length of time, and the demands upon all the hospitals are growinng.
>
> There are two reasons for this precarious position that we find our voluntary hospitals in now. One is the rising costs of food and services. For example, the raise in the price of meat two weeks ago increased the cost of meat for this particular hospital some $4,000 a month. The increase of a penny in the price of milk increased the cost $1,200 a month. Second, the loss incurred by the care of the sick poor of the city. This is of the greatest importance.
>
> The city pays the voluntary hospital $6 a day for city patients. The most efficient hospitals run a cost of between $11 and $12 a day for the care of such patients, creating a deficit of $5 to $6 per day. This strain is too great. It cost

the hospital used as an example in this article, $189,000 out of pocket, to care for these city patients in 1946, when the city paid $4.50 per day. The city raised the rate to $6 in 1947, but in spite of that it will cost this particular hospital in the neighborhood of $150,000 in 1947 to take care of city patients. The city administration is well aware of the difficulties. They are finding it in their own hospitals as well as the voluntary hospitals.

The total amount needed to bring the voluntary hospitals in approximate balance is not very large when considered in relation to other things and would not amount to much more than $5,000,000. The danger is that if costs are not covered, the voluntary hospitals will cease to function, in which case it will cost the citizens a great deal more to take care of the sick in public institutions than it does through the voluntary hospital system.

We have already discussed the rising costs to the public of medical services and surmise that this is only the beginning, not the end.[1]

If this city, like many another, can't take care of its own ailing let it say so. But do not let it keep up the pretense that it is doing so when actually it is asking private charity to shoulder half its burden and arrogating the credit to itself.

Do not let the average citizen be gulled into thinking that the city or state is taking care of him when it is not. Not when private charity is being bled white.

If there ever was a matter which should become one for public discussion, this is it. If our social system is going to change, very well. If the fountains of private charity are to be exhausted, perhaps that is inevitable. But we can at least put our cards on the table.

We cannot allow our system of voluntary hospitals and our long and honorable tradition of the best care for the sick poor by the best men of the medical profession, unremunerated, to be dragged down by the inadequacy of any system of socialized care that hasn't worked well, doesn't work well, and probably won't work well.

Are we to be forced to abandon a voluntary hospital system which is one of the proudest evidences we can present of the sense of obligation of our well-to-do people and be constrained to substitute a municipal or state system of socialized care which will then be pointed out as one of the most recent and most glaring evidences of the failure of private enterprise?

Editorial, *N. Y. St. J. M.*, January 15, 1948.

1 New York State J. Med. 47:2407 (Nov. 15) 1947; 47: 2663 (Dec. 15) 1947.

CANCER AND CHEMISTRY

In a recently published editorial, Charles Huggins expresses the opinion that at long last a beginning has been made in the treatment of advanced cancer by chemical means.[1] The tremendous progress in other departments of science, particularly in physics and chemistry, since 1941 has contributed heavily to advances made in the medical sciences. Progress in the mastery of disease must go hand in hand with more knowledge of the structure and function of normal tissues and organs. As advances against infectious diseases in previous decades were made step by step, so now the assault on cancer shows benefits, not along the whole front but only in a few specific types of tumors. In experimental work, the use of crude extracts and laboratory soups result in doubt, inaccuracy, and confusion. Investigators find the greatest rewards in experiments with pure chemicals.

The treatment of cancer is greatly handicapped by the lack of reliable clinical tests. Until more dependable tests for cancer are devised, it will be impossible to discern the slight or minute benefits (or harm) following the administration of any given therapeutic agent. At present the only valuable clinical tests of neoplastic activity are those for tumors of the blood-forming organs and for cancer of the prostate. Rapid and reliable information concerning the presence and extent of cancer is available from an examination of the circulating cellular elements in the blood in neoplasms of the hemopoietic tissues, and by determining the values of serum phosphatases in cancer of the prostate.

Chemical agents that seem to have some inhibiting effects on the growth of cancer may be divided into three groups: necrotizing agents, competitive inhibition, and nuclear damage.

Necrotizing agents. It has long been known that the products of certain bacteria, when administered parenterally, produce severe hemorrhage in the tumors within a few hours, with subsequent necrosis of malignant neoplasms. In a brilliant series of investigations, Shear and his co-workers have succeeded in separating the hemorrhage-producing agent in a cul-

1 Huggins, Charles: Editorial, Surg., Gynec. and Obst., Nov., 1947.

ture of Serratia marcescens (Bacillus prodigiosus) from the toxic and inert contaminants. Unfortunately, the necrosis is seldom complete and while some tumors regress, others usually remain viable. Further experiments with this more purified and powerful polysaccharide are necessary to determine its usefulness, if any, in the treatment of cancer.

Competitive inhibition. In cancer of the prostate, an essential for the nutrition of the malignant cells often is androgen. With androgen supplied in adequate amounts, the tumor grows vigorously. Conversely, the cells tend to wither when androgen is withheld (orchiectomy), or when estrogen is administered. Aside from radioactvie chemicals, the first agent of known chemical composition favorably to influence widespread cancer was estrogen. Also it was the first substance known to exert this effort when given by mouth. Both estrogen and orchiectomy may be regarded as nonspecific chemotherapeutic agents.

In male and female mice, compound E of Kendall, derived from the adrenal cortex, causes massive involution of lymphosarcomas. White and Dougherty have demonstrated that adrenal stimulation decreases the activity of lymphoid tissue. These biochemical observations are supported by the fact that 11-dehydro-17-hydroxycorticosterone has damaging effects on lymphomas.

Para-aminobenzoic acid is a substance essential to the growth of certain bacteria. The ability of sulfonamides (demonstrated by Wood and Fildes) to neutralize these beneficial effects of para-aminobenzoic acid is an illustration of competitive inhibition.

Nuclear damage. The injurious effects of irradiation on tissue cells, including the frequently observed mutations, are probably the action of the rays on the nucleic acids of the cell nucleus. Radioactive isotopes with a short period of decay may be used to apply soluble radioactive chemicals to tissues throughout the body. Huggins believes that "radio-active phosphorus has great value in chronic lymphatic and myelogenous leukemias and is probably the best therapeutic agent available for polycythemia vera."[1]

Since Lushbaugh demonstrated that the lymphocyte count of rabbits was reduced by the use of nitrogen mustards (B-chloroethyl amines), they have received systematic biochemical investigation. In some cases of Hodgkin's disease, regression has followed the therapeutic use of nitrogen mustard. Aside from those produced by radiant energy, the nitrogen mustards are the only agents known to produce mutations chemically.

Another drug capable of producing regression in cancer growth is ethyl carbamate (urethane). It delays cell division without great interference with respiration. Recently it has been shown that urethane reduces the growth of prostate cancer, particularly those in relapse after treatment with hormones. Since this toxic drug acts by pycnosis and is not antiandrogenic, it is a new weapon involving a new principle in the treatment of advanced cancer.

We suggest restraint of undue enthusiasm over optimistic reports of the results of chemitherapy in cancer. Aside from the conservative use of endocrines, it is well to remain critical and skeptical of results claimed for drugs having the power and potential dangers of necrotizing agents, radio-active isotopes, the nitrogen mustards, and urethane. Years must pass before these dangerous drugs can safely be used except in experimental laboratories and in clinics under strict control.

Editorial, *N. Y. St. J. M.*, January 15, 1948.

The Directory page for 1948 is presented in this issue. Read it carefully, note just what committees you yourself are on, and be ready when comes the call for service. We shall thank you to point out the errors on this page—promptly.

The unusual spectacle of reprinting three editorials from one journal is presented herewith. Having just read them (we hope), we feel sure you will agree that this unusual action is justified.

ARMY TRAINING FOR SPECIALTY BOARDS

1. The U. S. Army Medical Department announces the availability of opportunities for advanced training and experience in the various special fields of medicine and surgery in overseas Army hospitals. These hospitals are registered with the American Medical Association, and this training may be acceptable by the specialty board as part of the period usually required to be spent in limited practice and experience prior to admission for examination. Interested members of the medical profession who have completed the formal training requirements for certification in one of the special fields are eligible to apply for these positions. On 1 January 1948 the following opportunities will be available, and will be kept open until filled:

SPECIALTY	NO. OF OPENINGS
Eye, Ear, Nose & Throat	7
Obstetrics & Gynecology	14
Anesthesia	7
Ophthalmology	3
Otorhinolarynology	3
Neurosurgery	1
Orthopedic Surgery	5
Thoracic Surgery	1
Plastic Surgery	1
Radiology	11
Internal Medicine	24
Dermatology	3
Neuropsychiatry	15
Pediatrics	10
Cardiology	2
Pathology	1

There are also 21 positions in general surgery and 5 positions in urology, but these boards specify "supervised practice" and it has not yet been determined whether or not the hospitals will be approved by these boards. However, full approval of these specialties is being sought and inquiries are invited.

Positions offered will be in the following hospitals:

NAME	LOCATION	BED CAP.
97th General Hospital	Frankfurt, Germany	1000
98th General Hospital	Munich, Germany	1000
110th Station Hospital	Vienna, Austria	150
120th " "	Beyreuth, Germany	325
124th " "	Linz, Austria	150
130th " "	Heidelberg, Germany	250
250th " "	Regensburg, Germany	150
279th " "	Berlin, Germany	250
317th " "	Wersbaden, Germany	150
319th " "	Bremerhaven, Germany	600
385th " "	Nurnberg, Germany	350
387th " "	Stuttgart, Germany	453
388th " "	Giessen, Germany	250

These locations provide excellent facilities and equipment, a wealth of clinical material and the services of visiting consultants who are outstanding specialists in the various fields of medical practice. In addition, opportunities will be afforded to observe the work of notable scientists and physicians in German and Austrian Universities.

2. The applicant may avail himself of this training for periods of one, two or three years. Those applicants who are selected, and who hold reserve commissions in the Medical Corps, will usually be recalled to active duty in the highest grade attained prior to release from previous active service. Those who do not hold such reserve commissions will be tendered a reserve commission in the Medical Corps in keeping with their age, years of professional experience and prior service in any branch of the Armed Forces. Prior military service is not required. Individuals who are members of the U. S. Naval Reserve must transfer to the Army Reserve before being called to active duty. Families of married applicants will be allowed to accompany them to the place of duty. Suitable quarters are available. Families of individuals who do not declare their desire to serve for periods to exceed one year cannot be transported at Government expense.

3. Eligible physicians are invited to communicate with The Surgeon General, U. S. Army, Washington 25, D. C., for further information. Inquiries should include the following information: Name, address, age, nationality, marital status, dependents with age of each, medical school and graduation date, internship and date, details of graduate training, specialty and geographic location desired, contemplated length of service, details of prior military service.

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Alternates: I. J. MacCollum, John Martin.

Censor: W. C. Deakyne.

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